

## MEDICINE AND DENTISTRY

### 1. Introduction

Recent studies have shown a significant effect on the condition of the pancreas in patients with primary osteoarthritis (OA) [1–3]. It is known that the basis of endocrine disorders in chronic pancreatitis (CP) is the morphological features of the location of the islets among the acinar tissue, rather than isolated from it, which contributes to the interaction between exo- and endocrine cells of the pancreas [4]. Due to the peculiarities of the blood supply to the pancreas allocate insulo-acinar vascular system. In the pancreas, blood flow is directed from the islets to the exocrine tissue, which is one of the bases of functional interaction between the endocrine and exocrine tissues, i.e. pancreatic hormones affect its external secretion and vice versa [5]. In addition, changes in the pancreas of patients with CP with type 2 diabetes mellitus (DM2) often occur against the background of steatopancreatosis, which causes the progression of CP and diabetes mellitus [6–8]. Thus, the study of the functional capacity of the pancreas in CP in comorbidity with DM2 and OA is also relevant given that patients with this combination are associated with the presence of metabolic syndrome [9, 10].

**The aim of the study** was to investigate the state of functional capacity of the pancreas in patients with comorbid chronic pancreatitis and type 2 diabetes mellitus with osteoarthritis.

### 2. Material and methods

117 patients with CP with OA with concomitant DM2 and without it were studied. The main group consisted of 92 outpatients with CP with OA in combination with diabetes mellitus in the phase of stable or unstable remission, the comparison group – 25 patients with isolated CP with primary OA, and the control group – 30 healthy individuals. The comparison groups were comparable in age, sex, duration and treatment complex in the previous stages. Patients were registered with the Ternopil Center for Primary Health Care and were monitored during 2017–2020.

The materials of the clinical study were considered at a meeting of the commission on bioethics of the I. Horbachevsky Ternopil National Medical University Minutes № 60 from 01.09.2020. The work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). All patients signed an information agreement to participate in the study.

### INFLUENCE OF EXOCRINE PANCREATIC INSUFFICIENCY ON THE COURSE OF TYPE 2 DIABETES MELLITUS IN PATIENTS WITH PRIMARY OSTEOARTHRITIS

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**Abstract:** The study of the functional capacity of the pancreas in chronic pancreatitis (CP) in comorbidity with type 2 diabetes mellitus (DM2) and primary osteoarthritis (OA) is also relevant given that patients with this combination are associated with the presence of metabolic syndrome.

**The aim of the study** was to investigate the state of functional capacity of the pancreas in patients with comorbid chronic pancreatitis and type 2 diabetes mellitus with osteoarthritis.

**Material and methods.** 117 patients with CP with OA with concomitant DM2 and without it were studied. The main group consisted of 92 outpatients with CP with OA in combination with diabetes in the phase of stable or unstable remission, the comparison group – 25 patients with isolated CP with primary OA, and the control group – 30 healthy individuals. Diagnoses of OA, CP and DM2 were established according to generally accepted criteria and protocols

**Results.** Analysis of the data showed that on average in the contingent of studied patients with comorbid OA, CP and DM2 excretory insufficiency of pancreas was significantly more severe than in the group of patients with isolated CP with OA.

**Conclusions.** In the combined course of CP and DM2 with OA, the correlation between fecal  $\alpha$ -elastase-1 and glycosylated hemoglobin was statistically significantly stronger than in the group of patients with isolated CP, indicating a mutually aggravating effect of CP and DM2.

**Keywords:** primary osteoarthritis, chronic pancreatitis, type 2 diabetes mellitus.

The mean age was  $(47.54 \pm 9.51)$  years. There was a predominance of women over men (59.5 % and 40.5 %), and the largest share (72.4 %) were patients of working age – up to 65 years. The average duration of CP was  $(11.91 \pm 0.97)$  years, OA –  $(15.24 \pm 0.89)$  years, DM2 –  $(7.56 \pm 1.37)$ . Diagnoses of OA, CP and DM2 were established according to generally accepted criteria and protocols [4]. Assessment of the presence and depth of excretory insufficiency was performed according to the “gold standard” – determination of the content of fecal  $\alpha$ -elastase-1 by ELISA using standard kits from BIOSERV ELASTASE 1-ELISA. The evaluation of parameters was performed according to generally accepted international standards (normal pancreas function without ECN phenomena –  $>200 \mu\text{g/g}$ ) [5]. Analysis of the coprogram was performed to determine the presence of excretory insufficiency of pancreas and concomitant enterocolitis. The assessment was performed on a scale, where 1 point took into account pathological signs. To diagnose incretory insufficiency of the pancreas used to determine the level of fasting blood glucose, glycosylated hemoglobin (HbA1c) (using a kit for rapid determination of HbA1c by ion exchange chromatography) and the HOMA-IR index, calculated by the formula:

$$\text{HOMA} = (\text{fasting glucose (mmol/l)} \times \text{fasting insulin } (\mu\text{MO/l})) / 22.5. \quad (1)$$

The assessment of the state of the pancreas was performed according to the parameters of ultrasound examination of the pancreas, which were summarized to determine the severity of the process according to the criteria of the Marseille-Cambridge classification of CP in points.

The parametric distribution used Student's t test (t-test). For the populations whose distribution differed from the “normal”, nonparametric tests were used: to compare two independent samples of the Mann-Whitney U-test. Analysis of the relationship between the two traits in the presence of a normal distribution was evaluated by the results of Pearson's correlation analysis (r), with a distribution other than normal, a nonparametric Spearman's rank correlation method (R) was used.

### 3. Results

In the **Table 1** presented data on the functional and structural state of the pancreas in the comparison groups. Analysis of the data showed that on average in the contingent of studied

patients with comorbid OA, CP and DM2 excretory insufficiency of pancreas was significantly more severe than in the group of patients with isolated CP with OA on the content of fecal  $\alpha$ -elastase – respectively ( $109.25 \pm 1.21$ )  $\mu\text{g/g}$  and ( $163.39 \pm 3.45$ )  $\mu\text{g/g}$ , which corresponded to the medium and mild degrees of excretory insufficiency of pancreas, respectively, in the groups of comorbid with DM2 and isolated CP with OA ( $p < 0.001$ ).

**Table 1**

Comparative analysis of the functional and structural state of the pancreas of patients in the study groups depending on the presence of diabetes mellitus type 2

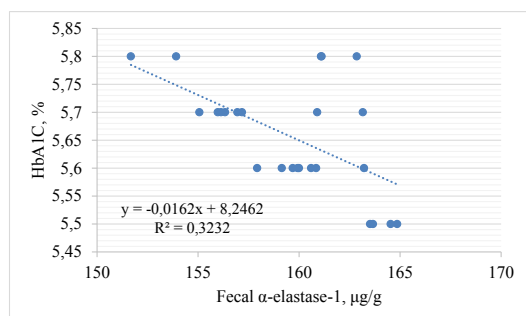
Indicator functional state of the pancreas	Comparison group		
	Control group (n=30)	Patients with CP (n=25)	Patients with CP and DM2 (n=92)
$\alpha$ -elastase, $\mu\text{g/g}$	$245.63 \pm 6.28$	$163.39 \pm 3.45^*$ $p_{2-3} < 0.05$	$109.25 \pm 1.21^{**}$
Blood glucose, mmol/l	$4.78 \pm 0.08$	$5.47 \pm 0.21^*$ $p_{2-3} < 0.05$	$8.91 \pm 0.31^{**}$
HbA1c, %	$4.55 \pm 0.10$	$5.64 \pm 0.12^*$ $p_{2-3} < 0.05$	$7.75 \pm 0.12^{**}$
HOMA index	$1.46 \pm 0.09$	$1.43 \pm 0.07$ $p_{2-3} < 0.05$	$3.27 \pm 0.06^{**}$
Coprogram score, points	$0.09 \pm 0.02$	$3.69 \pm 0.14^*$ $p_{2-3} < 0.05$	$5.62 \pm 0.11^{**}$
Ball ultrasound indicator of the structure of the pancreas, points	$1.05 \pm 0.03$	$3.99 \pm 0.68^*$	$6.22 \pm 0.66^{**}$

Note: \* – probable difference of indicators concerning such control groups ( $p_{1-2} < 0.05$ );

\*\* – probable difference of indicators in relation to those in the group with isolated CP with OA ( $p_{1-3} < 0.05$ )

An inexpensive but informative analysis, a coprogram, was also used to detect pancreas excretory dysfunction. We found a statistically significantly higher level of this indicator in patients with CP with DM2 compared with that in isolated CP with OA (respectively ( $5.60 \pm 0.10$ ) and ( $3.89 \pm 0.16$ ) points) ( $p < 0.05$ ).

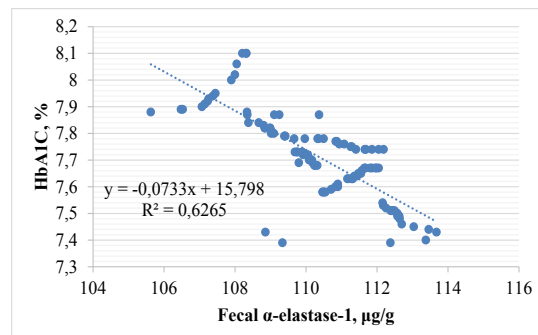
A correlation and regression analysis between faecal  $\alpha$ -elastase-1 and glycosylated hemoglobin was also performed, which showed the presence of statistically significant high strength of negative bonds in both study groups ( $p < 0.05$ ), in the group of patients with OA and CP without DM2 –  $r = -0.568$ , and in the group of patients with OA, CP and DM2 –  $r = -0.791$  ( $p < 0.05$ ) (Fig. 1, 2).



**Fig. 1.** Relationship between fecal  $\alpha$ -elastase-1 and glycosylated hemoglobin in patients with isolated CP with OA

Analyzing the results of the analysis, it was found that in the group of patients with CP and DM2 with OA the correlation was

statistically significantly stronger than in the group of patients with isolated CP, indicating a mutually aggravating effect of CP and DM2.



**Fig. 2.** Relationship between fecal  $\alpha$ -elastase-1 and glycosylated hemoglobin in patients with CP and DM2 with OA

#### 4. Discussion

Many studies have been found to investigate the effects of CP on DM2 [6, 7]. Lohr at al. have shown that exocrine pancreatic function is associated with incretory function of the pancreas [8]. Kothari at al. have shown that patients with CP have an increased risk of developing DM2 [5]. Many studies have been found on the effect of chronic diseases on the course of primary OA [3, 4, 9, 10]. However, we did not find any studies that investigated the effect of CP and DM2 on the course of primary OA.

Our data suggest that the comorbid course of CP, DM2, and primary OA have a mutually aggravating effect.

**Study limitations.** A limitation of our study is not too many indicators that we studied in the groups of patients during treatment and rehabilitation included in the study.

**Prospects for further research** – the development and justification of comprehensive treatment programs for patients with comorbid CP and DM2 with primary OA.

#### 5. Conclusions

1. With the comorbidity of CP and DM2 with OA excretory insufficiency of the pancreas was significantly more severe than in the group of patients with isolated CP, the content of fecal  $\alpha$ -elastase – respectively ( $110.35 \pm 1.81$ )  $\mu\text{g/g}$  and ( $159.56 \pm 4.15$ )  $\mu\text{g/g}$ , which corresponded to the average and mild degrees of excretory insufficiency pancreas, respectively, and the score of the coprogram – respectively ( $5.60 \pm 0.10$ ) and ( $3.89 \pm 0.16$ ) points  $p < 0.05$ ).

2. The presence of statistically significant high strength of negative relationships between the parameters of fecal  $\alpha$ -elastase-1 and glycosylated hemoglobin in both study groups ( $p < 0.05$ ): when CP with OA without DM2 –  $r = -0.568$ , when comorbidity of CP and DM2 –  $r = -0.791$  ( $p < 0.05$ ), which proved a significant interaction between the state of excretory and incretory functions of the pancreas.

3. In the combined course of CP and DM2 with OA, the correlation between fecal  $\alpha$ -elastase-1 and glycosylated hemoglobin was statistically significantly stronger than in the group of patients with isolated CP, indicating a mutually aggravating effect of CP and DM2.

#### Conflict of interests

The authors declare there is no conflict of interests.

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